REMARKS/ARGUMENTS

An Information Disclosure Statement is submitted herewith.

Claims 1-5, 8-25 were pending at the time of the Office Action. Claims 8-18, 21, 23 and 25 are withdrawn due to a restriction requirement.

Claim 1 is amended to clarify that the viable hybrid cell is a zygote cell, that the donor and recipient cells are mammalian cells, and that the recipient cell is an oocyte, a zygote, or a cell from a two-cell embryo. Support is found throughout the specification and original claim 2.

Claim 1 is also amended to correct an informality.

Claim 2 is canceled.

Claim 19 is amended to clarify that the hybrid cell is a zygote cell.

Claim 20 is amended to refer to claim 19 rather than claim 17. Although previously included in restriction Group III, the amendment places claim 20 into Group I. Therefore, claim 20 is under consideration. Claim 20 is also amended to clarify that an animal is a nonhuman animal, and has a single functional mitochondrial population.

Claims 22 and 24 are each amended to refer to claim 21. Although previously included in restriction Group I, the amendments place claims 22 and 24 into Group IV. The amendments to claim 24 renders the 35 USC § 101 rejection to this claim as moot.

35 USC § 112 Rejections

Current claim 1 recites that the donor and recipient cells are mammalian cells. Thus, the rejection to claims 1, 3-5 and 19 as non-enabled are moot.

The amendments to claims 22 and 24 render the 35 USC § 112 rejections to these claims as moot.

35 USC § 102 Rejections

The rejection of claim 19 as anticipated by Meirelles et al. is respectfully traversed. "To anticipate a claim, the reference must teach every element of the claim." MPEP § 2131. In the present case, Meirelles et al. fails to achieve this standard.

Current claim 19 involves a method of producing a viable hybrid zygote cell having a single, functional mitochondrial population. Meirelles describes a hybrid zygote formed by fusion of an enucleated oocyte with a single blastomere derived from a morula. There is no teaching in Meirelles to deplete the mitochondrial DNA (mtDNA) population of the blastomere before fusion with the oocyte. As a result, the hybrid

zygote cell formed in the process of Meirelles will inevitably contain two mitochondrial populations, derived from host and donor cells respectively. It is well known that cattle are heteroplasmic due to two populations often being present in oocytes. These can be transmitted through to the offspring randomly, thus no two offspring would likely have the same levels of heteroplasmy. Moreover, the donor cell has been fertilised. Therefore, by using donor cells derived both maternally and paternally, the paternal mtDNA may not have been eliminated especially if the sperm and oocytes were from slightly diverse sources such as cross-breeds, or they were used before the 8-cell stage of preimplantation development, when the sperm is eliminated in same breed crosses. Thus the method of Meirelles could in fact result in 3 mtDNA populations in the zygote, including mtDNA derived from the sperm used to fertilise the donor cell.

In contrast, the method of the present application involves depletion of the mtDNA population from the donor before fusion, such that the hybrid cell formed will necessarily have only a single mitochondrial DNA population. As such, the hybrid cell of Meirelles would not be producible by the method of the present application.

It is noted that the zygotes of Meirelles are implanted into recipient heifers and grown to term, and that some of the animals produced had cells containing only a single mitochondrial population. Such mitochondrial homoplasmy occurs because mtDNA from the donor is gradually eliminated after the embryo reaches the 8-cell stage (as described in the paragraph bridging columns 1 and 2 of page 353 of Meirelles). As such, it is implicit that all of the zygote cells produced by the method described in Meirelles will have mtDNA from both donor and host cells. This method will therefore result in animals in which the donor mtDNA has been eliminated from some, but not all of the tissue types. In contrast, the cells claimed in the present application will grow into animals in which all tissue types will necessarily have only a single functional mitochondrial population. Claim 20 is therefore also distinguished over Meirelles.

The rejection of claims 1, 3 and 5 as anticipated by Levy et al. is respectfully traversed. Levy et al. fails to teach all elements of the claims. Current claim 1 recites "wherein the recipient cell is an oocyte, a zygote, or a cell from a two-cell embryo." There is no disclosure in Levy et al. of the use of an oocyte, zygote, or two-cell embryo cell as the recipient cell. Therefore, claims 1, 3 and 5 are not anticipated by this reference.

35 USC § 103 Rejection

The rejection of claims 1 and 4 as obvious over Sims et al. and Levy et al. in view of Hiendleder et al. is respectfully traversed. "To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F. 2d 981, 180 USPQ 580 (CCPA 1974); MPEP § 2143.03. In the present case, the prior art does not meet this standard.

Although Levy does discuss the production of hybrid cells, the chief aim of that document is the production of chimeric animals (as for example stated in the title of the

document). This is achieved by the injection of hybrid cells into blastocysts which are then allowed to develop. A chimeric animal inevitably has mixed mtDNA populations.

The disclosure of Sims is simply a standard prior art method of cloning by nuclear transfer, as discussed in the introduction to the present application. In Sims' case this is achieved using an oocyte as the recipient cell. However, in view of the aim of Levy being the production of a chimeric animal, as stated above, there is no motivation whatsoever for the skilled man to combine the teaching of Sims with that of Levy. In particular, the benefit achieved by the method of Sims (namely the production of a totipotent hybrid cell) is irrelevant when, as in Levy, it is intended to insert that cell into a blastocyst.

Furthermore, claim 1 of the present application requires the production of a cell with a single functional mtDNA population. In contrast, Levy teaches the use of mutant mtDNA, thereby producing a population which is non-functional. Thus, Levy actually teaches away from the invention of the present application.

In contrast to the disclosure of Levy, the present application offers the benefit of producing an animal with a single genetic population, rather than a chimera. It is impossible to predict, in the method of Levy, which tissues of the final animal will contain the genetic information from the hybrid, and which will contain the original genetic information from the blastocysts into which the hybrid was injected. Thus, in order to carry out further studies on the tissue resulting from the hybrid, it would first be necessary to carry out extensive dissection and analysis in order to identify the hybrid tissue. By contrast, the invention of the present application produces animals having only a single mitochondrial and nuclear genetic population in all tissues (i.e. a truly homoplasmic animal).

Not only does the combination of Sims and Levy fail to teach the present invention, Hindleder does not even provide the motivation to make such a combination. Hindleder does not mention depletion of donor mtDNA but rather that the main complement of mtDNA should be from specific mtDNA genotypes and this would be the composition in the recipient oocyte. The selection of mtDNA specific genotypes is very different to homoplasmy.

For each of the foregoing reasons, claims 1 and 4 are not obvious.

In view of the foregoing amendments and remarks, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

A Petition and fee for a 1 month extension of time is submitted herewith.

No other fee is believed due. However, the Commissioner is hereby authorized during prosecution of this application and any related appeal, to charge any fees that may be required (except for patent issue fees required under 37 CFR §1.18) or to credit any overpayment of fees to Deposit Account No. 50-0337. If an extension of time is required in connection with this paper, please consider this a Petition therefor and

charge any fees required to Deposit Account No. 50-0337. Please ensure that Attorney Docket No. LA-7492-102/10408733 is referred to when charging any payments or credits for this case.

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Respectfully submitted,

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